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Metal Ion Complexes of Amino Acids.
Part III. A Reconsideration of the Copper(II) Complexes of D-Cycloserine

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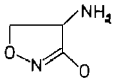
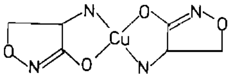
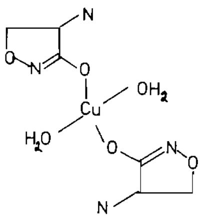
The antibiotic D-cycloserine (D-C.S.) (I) has the obvious ability to chelate metal ions [1]. There have been only two reports on the coordination chemistry of this substance [2, 3]. In the most recent of these green and purple copper(II) complexes were obtained in aqueous solution. It was suggested that these were a ring open green form (II) and a ring closed purple form (III). In this note a more plausible explanation for these results is presented together with the synthesis of a new solid 1:1 complex of copper(II) and D-cycloserine [Cu(D-C.S.)]$ClO_4 \cdot 4H_2O$.







Sakurai's observations that solutions in Tris buffer of copper(II) and D-cycloserine are initially green and turn purple/blue after a few days was readily confirmed. The buffer Tris is a fairly good ligand [4] and may well have involved itself in coordination to copper(II) and complicated the results. However solutions prepared from copper(II) sulphate pentahydrate and D-cycloserine in 1:1 to 1:5 ratios at various values of pH in the range 6.00 to 8.00 showed exactly similar behaviour. Solutions prepared from copper(II) acetate monohydrate and D-cycloserine (1:2) were also initially green and turned blue/purple in 2–3 days; heating such solutions caused the change to become rapid.

The blue complex finally formed had in both the solid state and solution properties similar to other simple bis-amino acidates [5] of copper(II). Our own work and that of Sakurai agrees on this point (Table I). This note will concentrate on the properties of the green solutions and a new solid complex precipitated from such solutions.

The structure of D-cycloserine (I) suggests that it might form a stable 1:1 polymeric species (IV):

$$N(\text{CuD-C.S}) \rightleftharpoons (\text{CuD-C.S.})_N$$

A green solution approximately 0.1 molar in both copper(II) (from $CuSO_4 \cdot 5H_2O$) and D-cycloserine was prepared; excess concentrated sodium perchlorate was added. The resulting solution was titurated with acetone; a green complex of empirical

TABLE I. Analytical Results and Spectroscopic Properties of the Complexes.

Compound	C	H	N	ϵ_{max} nm	g_{av}	
$Cu(D\text{-}C.S.)_2 \cdot 2H_2O$	23.88	4.68	18.57	–	–	Calculated
	23.82	4.71	18.11	573[a]	2.110	Ref. 1.
	–	–	–	570[b]	2.113	This work
Cu(D-C.S.) green solution	–	–	–	–	2.109	Ref. 1.
	–	–	–	670[c] 680[d]	2.098[c]	This work
$Cu(D\text{-}C.S.)ClO_4 \cdot 4H_2O$	10.71	3.89	8.33	–	–	Calculated
	10.47	3.64	7.96	718[b]	–	This work

[a] Solid, KBr disc. [b] Solid, diffuse reflective maximum of a single peak between 350 and 2500 nm. [c] Freshly proposed solution of green complex. [d] Freshly mixed $CuSO_4$ and D-C.S. solutions.

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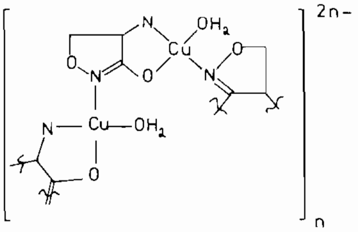
formula [(Cu D-C.S.)] $ClO_4 \cdot 4H_2O$ (Table I) precipitated as a fine powder. This was filtered off at the pump and washed with several aliquots of ice water. The properties of this complex in solution are similar to those reported for green solutions by Sakurai (Table I). The infra-red spectrum revealed a strong broad band due to perchlorate ~1100 cm^{-1} and normal 'ring closed' coordination of the amino acid is suggested by the presence of ν_{as} ~1610 cm^{-1}. The weaker ligand field is in line with a first coordination sphere of N_2O_4 made up of two nitrogens, a corresponding carboxylate and a water molecule (IV).



In conclusion the synthesis of the 1:1 green complex [Cu(D-C.S.)] $ClO_4 \cdot 4H_2O$ and the similarity of its properties (both in the solid state and solution) to freshly prepared copper(II) D-cycloserine solutions previously described, suggests that complexes of this stoichiometry may account for the initial green colour of such solutions. In view of the kinetic lability (and in particular the rate of ring closure) of copper(II) [6], ring open structures are extremely unlikely. Polymerization (IV) of the complex may explain the unusual properties of this system. Further studies of the kinetics controlling the interconversion of these complexes are anticipated in the near future.

References

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